

CHEMICAL INJURIES OF THE EYES

by

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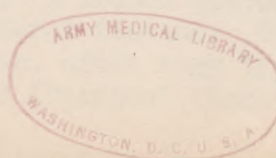
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It would be an impossible job to outline the characteristics and treatment of every type of chemical burn of the eye during an hour's lecture. Also, I doubt if you would bear up under the repetition which would result. During the early part of our work, we injected almost every chemical in the laboratory into the rabbit's cornea, and found many of these widely varying substances produced the same clinical and pathologic type of reaction. This is probably due to the fact that at least many of the characteristics represent how the eye reacts to the death of its cells, irrespective of the type of chemical injury. It might be worth while here to mention some of the peculiarities of reactivity which the anterior ocular tissues possess.

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FIG. 1

NORMAL HISTOLOGY AND PHYSIOLOGY OF THE CORNEA IMPORTANT IN CHEMICAL BURNS

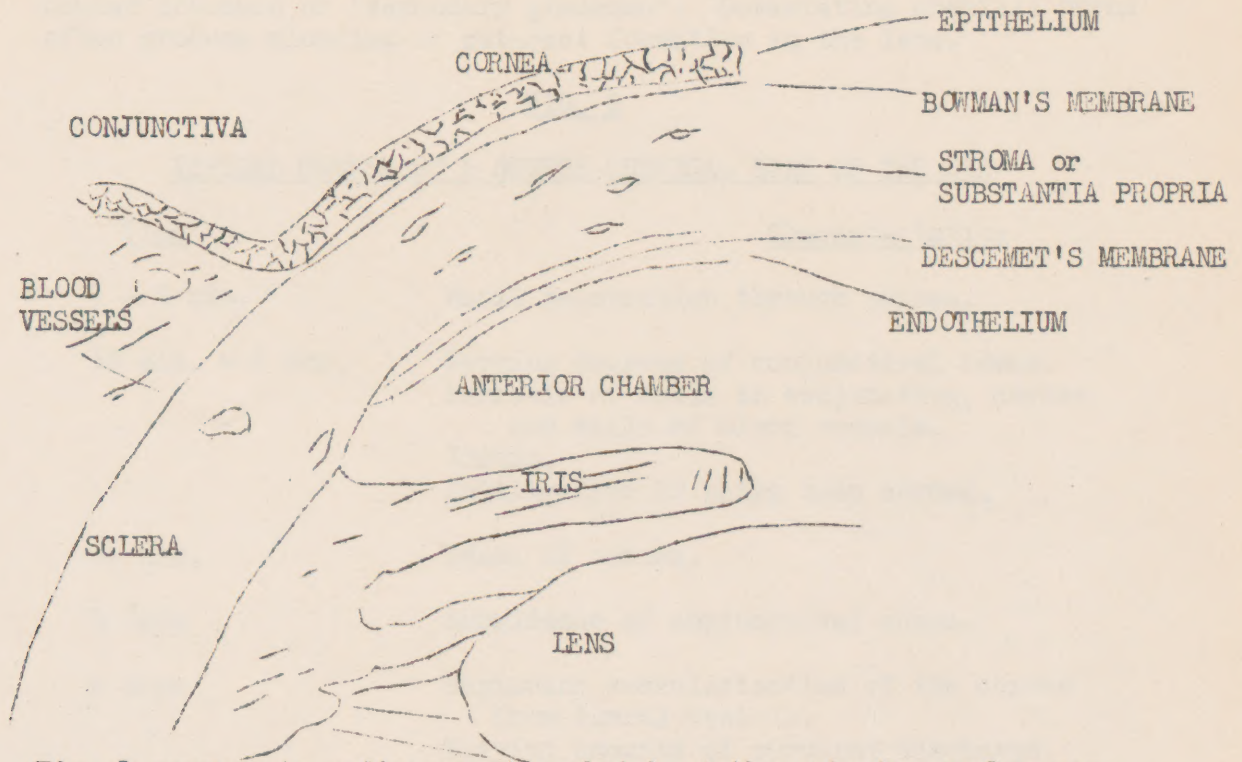
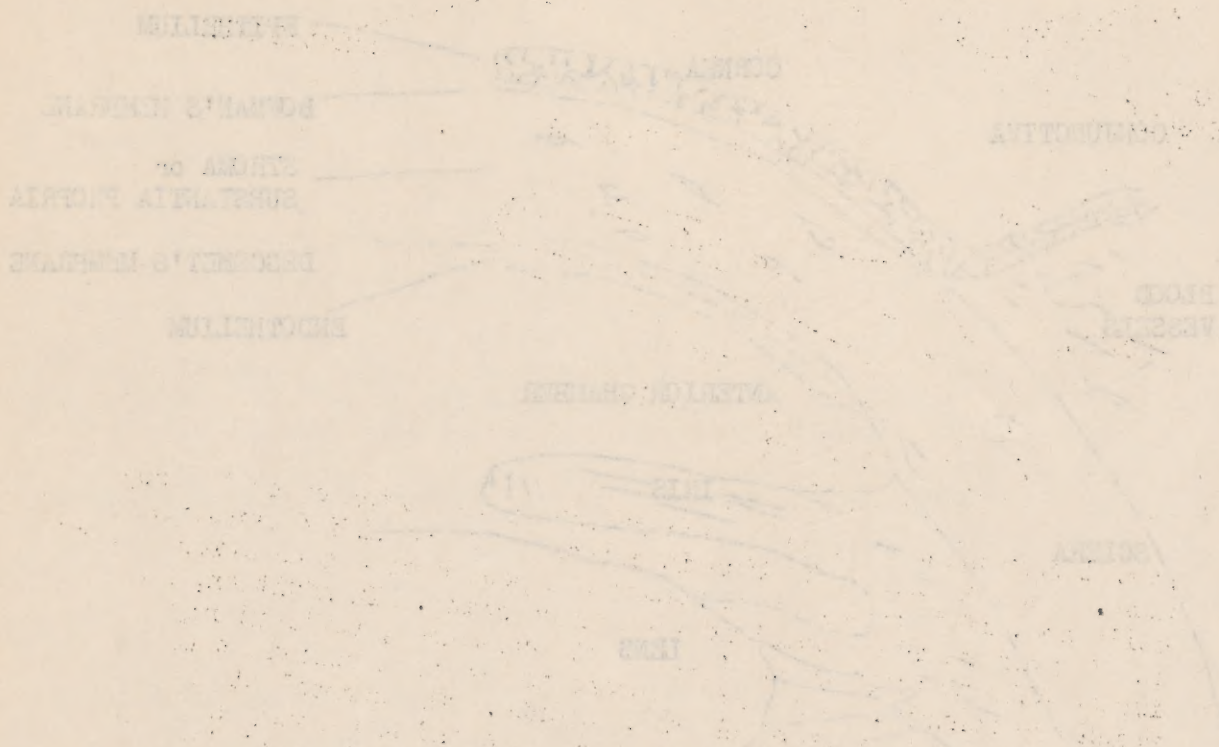


Fig. 1 represents a diagrammatic sketch of the anterior ocular segment. The corneal epitholium is composed of stratified squamous cells and, if damaged, shows remarkable powers of regeneration without leaving any residual opacification or scarring. In addition, it is impermeable to many types of chemical substances, particularly those which are ionized. Bowman's Membrane is somewhat resistant to trauma and the penetration of chemical agents. The corneal stroma or substantia propria contains very few cells and has a very sluggish metabolism. Defects in the stroma are healed by the proliferation of fibrous tissue, resulting in an opaque scar. Descemet's Membrane is tough and may remain clear for a short time while the anterior layers of the cornea slough off following a chemical injury. If the single layer of endothelial cells beneath Descemet's Membrane is damaged in any manner, the aqueous from the anterior chamber diffuses into the corneal stroma and produces edema. Edematous thickening of the cornea is almost a constant finding in all types of penetrating chemical injury to the cornea, and has been well correlated with damage to the endothelium in many of these cases.

Within the meshes of a rather loose sub-epithelial tissue are located the superficial conjunctival blood vessels, often necrotized and thrombosed by the chemical burn so that the surrounding tissue becomes ischemic. A second network of vessels lies more deeply within the cornea-scleral tissues. Ordinarily the cornea has no blood supply. However, after many types of injury, vessels may invade the cornea stroma ("pannus" formation).

The iris is usually involved in severe chemical burns of the

FIG. 1. HISTOLOGY OF THE CORNEA IN A NORMAL STATE



The cornea is a transparent, avascular tissue. It is composed of several layers. The outermost layer is the epithelium, which is a stratified squamous epithelium. Below the epithelium is Bowman's membrane, which is a thin, transparent layer. The middle layer is the stroma, which is composed of a dense network of collagen fibers. The innermost layer is the endothelium, which is a simple squamous epithelium. The cornea is avascular, meaning it does not contain any blood vessels. It receives its nutrients from the aqueous humor of the anterior chamber and the vitreous humor of the posterior chamber. The cornea is responsible for refracting light entering the eye.

Within the stroma of a normal cornea, the collagen fibers are arranged in a regular, parallel pattern. This arrangement allows light to pass through the cornea without being scattered. The collagen fibers are composed of a repeating unit called a tropocollagen molecule. These molecules are linked together to form a triple helix structure. The triple helix structure is what gives the collagen fibers their strength and stability. The cornea is a very strong tissue, and it is able to maintain its shape under pressure.

eye. Inflammatory debris can produce adhesions between the iris and lens ("posterior synechiae"), or block the normal drainage of aqueous from the eye via Schlemm's Canal located in the angle of the anterior chamber. Such complications readily lead to a rise in intraocular pressure or "secondary glaucoma". Devastating chemical burns often produce clouding or cataract formation in the lens.

FIG. 2

TYPICAL COURSE OF A SEVERE CHEMICAL BURN OF THE EYE

<u>Time</u>	<u>Characteristics</u>
1 - 5 min.	Rapid penetration through cornea.
10 min. - 8 hrs.	Varying degrees of conjunctival edema. Necrosis of cells in conjunctiva, cornea and walls of blood vessels. Iritis, Infiltration of polys into cornea.
24 hrs.	Edema of cornea.
3 days	Subsidence of conjunctival edema.
6 days	Beginning vascularization of the cornea from limbal vessels. Varying amounts of purulent discharge and secondary infection.
8 - 13 days	Varying degrees of corneal ulceration. Subsidence of corneal edema. Scar tissue repair.
14 days and over.	Permanent corneal opacification. Complications: perforation of cornea, recurrent ulcerations, panophthalmitis, phthisis bulbi, glaucoma, cataract, symblepharon.

The above table represents roughly the chronologic steps in the reaction of an eye to a necrotizing chemical. This sequence of events will be found illustrated many times during the discussion of varied types of chemical injury.

There are, however, three main classes of chemical injury to the eye:

1. Non-progressive burns: e.g. acids.
2. Progressive lesions: e.g. alkalis
sulfur dioxide
indelible dyes
vesicant war gases.

3. Irritative chemicals: e.g. lacrimators.

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ACID BURNS. The severity of the lesion produced by acid is dependent on several factors. (1) Character of Anion. For comparable concentrations and exposures, the pH must be lower than 2 to produce a lesion with hydrochloric acid, lower than 4 to produce a lesion with acetic acid, whereas damage is produced at neutrality by tannic acid. These facts might be explained by a difference in affinity on these anions for the corneal proteins. (2) Degree of Dissociation or pH of the Acid. Hydrochloric acid will produce more damage than the same concentration of acetic acid. (3) Concentration of the Acid. (4) Duration of the Exposure.

The corneal opacification following exposure to caustic acids is not progressive, and so one can almost predict the amount of residual damage which will result by observing the case soon after the injury.

This histological section shows a rabbit's cornea 8 hours after a 10-minute irrigation with N/10 HCl. The most interesting feature is a sharp line of demarcation between the pyknotic cells of the burned portion of the cornea and the normal cells immediately adjacent.

Treatment. Since penetration of the acid into the eye takes place rapidly, the primary consideration in early treatment is the immediate removal by copious irrigations of any acid remaining on the surface of the eye. The choice of irrigating fluids is less important than speed of instituting treatment. If a 1.5% solution of sodium bicarbonate is not at hand, the eyes should be washed out with water. Later treatment is symptomatic, and consists of argyrol 10% followed by boric acid irrigations to remove any mucopurulent discharge, and the instillation of liquid petrolatum or a bland eye ointment (e.g. 2% boric acid; bichloride of mercury 1:10,000; merthiolate 1:5000, etc.). The application of a pressure bandage aids in splinting the lids, thus facilitating the regeneration of the corneal epithelium.

ALKALI BURNS. Ocular burns by alkalies are frequently seen in both civilian and army life: e.g., lime used in plastering and latrines, and lye and ammonia used domestically. These lesions are progressive and in this respect resemble burns by sulfur dioxide (commonly used refrigerator fluid), indelible dyes (e.g., gentian violet, crystal violet, etc., used for indelible pencils), and vesicant war gas, N-Mustard and Lewisite). The severity of alkali burns depends on several factors: viz. (1) pH. The rabbit's cornea, similar in tolerance to that of human beings, is damaged by solutions more alkaline than pH 11.0. (2) Concentration. (3) Duration of Exposure. This is important in burns by solid lye or lime, in which a small solid particle may lodge underneath the upper lid and act as a source of

alkali for several hours, Character of the Cation. This is of relatively little importance because similar progressive lesions are produced by a lime burn (calcium ions), lye burn (sodium or potassium ions), or ammonia (ammonium ions).

Clinical and Pathological Course. (Slide #3) Five hours after a mild lye burn, there is some milky necrosis and congestion of the conjunctiva with only a mild haziness of the cornea. (#3a) This kodachrome photograph was taken one month after the injury shown in the previous slide. Within the area which initially showed very little involvement can be seen a definite corneal infiltration which stains with fluorescein (i.e., the overlying epithelium is damaged). A small tongue of blood vessels extends out from the corneo-scleral margin to the infiltrated area. Such late infiltrations and vascularization of the cornea are frequently seen after alkali burns, and accordingly make the prognosis unpredictable. (#3b) This photograph was taken 5 hours after a severe lye burn. There is moderate edema of the conjunctiva with necrosis and ischemia at the corneo-scleral margin. The cornea is cloudy and the epithelium has been desquamated. (#3c) This eye sustained a severe lye burn three weeks previously. Many blood vessels have begun to grow into the cornea, and a few adhesions can be seen between the lids and globe (i.e., symblepharon). (#3d) This is a distressing example of the end results of a severe lime burn. The conjunctiva has over-grown the cornea, and there is a complete symblepharon.

(#4) This is the histological picture of a rabbit's cornea taken 10 minutes after a 10 minute irrigation with N/20 NaOH. The epithelium has been entirely lost. There is a washed-out appearance in the affected portion of the corneal stroma. (#4a) This section, also 10 minutes after exposure to NaOH, emphasizes the speed of penetration through the cornea. The alkali has penetrated through all the layers of the cornea and has damaged the endothelium on the posterior surface. (#5) Sections at 8 hours show an infiltration of polys into the cornea, a loss of stromal cells, and serum in the anterior chamber from the associated iritis.

Treatment of Alkali Burns. The chronologic sequence of treatment may be outlined as follows:

1. Irrigation of the eye for 5 minutes with water or any immediately available non-irritating solution should be performed. A buffer solution will neutralize any small particles of alkali which might remain hidden in the recesses of the conjunctival sac. The solution should not have a pH lower than 4.5 and should be isotonic. The following formula will satisfy these requirements:

Acetic Acid	2.5 gm
Sodium Acetate	3.0 gm
Sodium Chloride	4.5 gm
Distilled Water	1000.0 cc

It should be emphasized that time should not be lost in an attempt to obtain such a buffer solution if it is not readily at hand, but that irrigation with water be used instead. There is little satisfactory evidence that calcium ions per se have any detrimental effect on the cornea, and their attempted removal after lime burns with neutral ammonium tartrate solutions is probably valueless.

2. The upper lid should be everted and a thorough search made for any remaining solid particles of alkali which might be hidden in the upper cul-de-sac (lid fold).

3. Many European oculists recommend the immediate surgical removal of all necrotic and ischemic conjunctiva (white areas devoid of blood vessels). These denuded areas are then covered with mucous membrane grafts from the mouth ("Denig Grafts"). This procedure has been widely and successfully used in Europe, whereas the conservative treatment of alkali burns has been reported by other clinics to be equally efficacious.

4. Symptomatic Measures: atropine sulfate 1% solution or ointment three times a day for the associated iritis, argyrol 10% with boric acid irrigations to remove the mucopurulent discharge, oily drops or bland ointments, frequent breaking of early symblepharon adhesions, and a mild pressure bandage. In order to lessen the likelihood of secondary infection, the use of 5% sulfathiazol or sulfadiazine ointment (white petrolatum base) or microcrystalline sulfadiazine may be tried experimentally. The use of these substances should be discontinued if they appear to irritate the eye.

MUSTARD GAS (CICH_2CH_2)₂S ("HS").

Incidence of Mustard Gas Injuries to the Eyes (1917-18).

75-90% of all mustard gas casualties have ocular involvement.

1. Mild Conjunctival Irritation (75%):
Redness of conjunctiva between the lids.
Recovery in 1-2 weeks.
2. Severe Conjunctival Involvement (15%):
Horizontal band of white chemosis between the lids.
"Orange-peel" roughening of the cornea.
Complete recovery in 4-5 weeks.
3. Corneal Involvement (10% or less):
Produced by prolonged exposure to a concentration of mustard vapor as low as 1:10,000,000, a 30-60 second exposure to saturated mustard vapor at room temperature, or a splash burn with 0.0002 cc. of liquid mustard.

Marked photophobia, blepharospasm, conjunctival redness and edema.

Cornea stains with fluorescein (2% solution).

Iritis.

Recovery with residual corneal opacification after 2-3 months.

Tendency for relapsing and recurrent lesions.

The high incidence of mustard injuries to the eye is probably related to two factors: (1) moisture facilitates the penetration of mustard into the skin, and probably also into the eye, and (2) the sebaceous secretion of the mucous glands in the lids tends to concentrate lipid-soluble mustard vapor on the lid margins and in the eye. It has also been found experimentally that if a person is exposed to mustard vapor, the eyes will usually become affected before the skin (Reid).

The above customary division of mustard casualties into three grades of severity is important in regard to prognosis and therefore in the disposition of the patient at the casualty clearing station. The patients with corneal involvement should be directed to the base hospital for treatment under the direction of an ophthalmologist. The prognosis is fairly predictable within 24 to 48 hours after the exposure. It must be remembered that there is a latent period of 2-24 hours between the time of exposure to mustard vapor and the onset of symptoms. Liquid mustard, on the other hand, produces symptoms of irritation and burning almost immediately after contact with the eye. Should mustard be sprayed from the air during the present conflict, the incidence of severe lesions of the eye will undoubtedly rise. The size of droplets which are used routinely to produce severe mustard burns in rabbits are no larger than might be expected from a fine mustard spray in chemical warfare.

(Slides #9-13) These pictures were made during the last war of cases with mild conjunctival irritation and severe conjunctival involvement described above. About 75 or 100 cases have been reported in which patients, who originally sustained severe mustard burns of the cornea, developed recurrent corneal ulcerations and ocular irritation years later.

Clinical Appearance of Severe Mustard Lesions in the Rabbit. A series of kodachrome photographs has been taken to illustrate the progressive nature of an ocular burn in the rabbit produced by 0.0002 cc. of liquid mustard. Within 5 hours after the application, a small amount of white chemosis and ischemia develops at the site of the application, with a slight haziness of the adjacent cornea. After 18 hours, a marked conjunctival edema and congestion of vessels is present. At 24 hours, some petechial hemorrhages can be detected in the conjunctiva. These are probably due to a direct necrotizing action of mustard upon the walls of the blood vessels. At this same time, the corneal epithelium has become loose and in one area has desquamated off completely. Such a denuded area stains bright green with fluorescein. Mild edema of the corneal stroma can be detected by examination with a slit lamp. The clin-

ical picture after 8 days shows a subsidence of the conjunctival reaction and a further progression of the corneal ulceration and edema. A superficial blister of the cornea can often be detected, not unlike that found after a vesicant burn of the skin. Extending into the deeper portions of the corneal stroma from the corneo-scleral margin are a sheaf of blood vessels. These continue their extension into the cornea until all of the opaque cornea has become vascularized. The superficial conjunctival vessels have been thrombosed, and so there is no superficial vascularization of the cornea after this type of burn. A peculiar feature of mustard burns lies in the fact that, after 4 or 5 days, the edema of the cornea partially subsides and the opacification appears somewhat less. However, after 8 to 10 days, extensive vascularization, ulceration and vesicle formation presents a more distressing picture. After 2-3 weeks, ulcerated areas heal with the formation of an opaque scar well supplied with blood vessels. If these scars are observed over the course of several months, minute ulcerations can be seen to develop from time to time. These are thought to be due to the formation within the scar of cholesterol-like crystals which subsequently ulcerate through the surface of the cornea.

Vapor burns of the rabbit's eye are not unlike those produced by liquid mustard. Lesions of similar severity to those described above were produced by exposure of a rabbit's eye for 1 minute to a saturated vapor of mustard at 23°C.

Pathology of Mustard Burns of the Rabbit's Cornea. Within 2 hours after the burn with liquid mustard, there is marked edema of the conjunctiva and slight edema of the corneal epithelium. At 18 hours, the conjunctiva has become richly infiltrated with polymorphonuclear cells. The corneal epithelium shows definite necrosis and the stroma is somewhat edematous. At 30 hours, the conjunctiva shows signs of disintegration, and there is well-marked differential staining of the corneal stroma due to the necrosis. Polymorphonuclear cells begin their migration from the corneo-scleral margin into the substance of the cornea. After 7-10 days, blood vessels can be seen entering the corneal stroma at the periphery. Processes of repair with a heavy ingrowth of fibrous tissue can be detected after 2-3 weeks.

Treatment of Mustard Injuries of the Eyes: There are several facts which can be gathered from the clinical and pathological studies of mustard burns that provide a rationale for treatment.

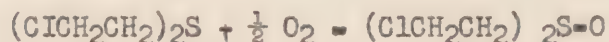
Time of Effective Treatment. Mustard has been shown to penetrate rapidly into the tissues of the eye. Toxic material has been demonstrated in the aqueous within 15 minutes after exposure to mustard. In addition, no residual toxic material can be found on the surface of the cornea after 5 minutes have elapsed. Thus we have rapid disappearance of mustard from the surface of the eye into the tissues. From the standpoint of the treatment of vapor burns, this

is particularly unfortunate, because there is a latent period of 2-24 hours after exposure before the onset of symptoms. In other words, the vesicant has penetrated into the tissues and probably caused some damage before the victim has become aware of his condition. This emphasizes the importance of immediate prophylactic use of the gas mask when the presence of mustard gas is suspected, and the futility of attempting to decontaminate the surface of the eye after vapor burns. The instillation of liquid mustard in the eye produces pain almost at once, and the individual is therefore warned of his exposure and can institute treatment immediately. Liquid mustard will not penetrate glass, and so these serious lesions produced by droplets of mustard spray can be prevented by the wearing of spectacles.

Irrigations. Much of the residual liquid mustard can be removed if the eye is thoroughly irrigated within 1-3 minutes after exposure. For this purpose, water is found to be as effective as other more complicated solutions.

Neutralizing Agents. No satisfactory neutralizing agents have been found. Mustard can be inactivated in the test tube by chlorination; e.g., with a 0.5% solution of dichloramine-T ($\text{CH}_3\text{C}_6\text{H}_4\text{SO}_2\text{NCl}_2$) in an organic solvent such as chlorinated liquid paraffin. This solution is effective for use in the eye during the first few minutes after a burn with mustard, but is not notably more efficient than water. The use of chlorinated solutions later will irritate the eye.

Mustard can be oxidized slowly in vitro by solutions of hydrogen peroxide, potassium permanganate, and sodium hypochlorite which will be tolerated by the eye.



Solutions of these low concentrations are no more effective than water for the treatment of mustard burns. Moreover, the use of excessively high concentrations or prolonged irrigations with these oxidants can in themselves produce devastating lesions of the eye. The normal eye will tolerate 2 drops of 0.5% hydrogen peroxide or 1% potassium permanganate. The use of 1% sodium hypochlorite accentuates the damage which mustard produces in the eye. Bleaching powder, recommended for skin decontamination, must not be used in the eye.

Livingston and Walker, 1941, suggested the use of intravenous vitamin C for the treatment of mustard burns of the eye, following experiments on a small series of rabbits. However, Mann and Pullinger later showed that the technique of application of mustard used by the above investigators was subject to great variation, and that the intravenous use of vitamin C did not alter the course of a mustard burn.

Oil Solutions. Liquid petrolatum and cod liver oil have been suggested for instillation in the eye after exposure to mustard. If this is done while the victim is still exposed to mustard vapor, these

solutions merely act to concentrate more mustard in the eye. Also, a prematurely early instillation of an oily substance tends to spread the mustard over the corneo-scleral junction. More severe reactions are produced when mustard is applied to this region of the eye. To prevent the development of symblepharon, the instillation of oil drops or a bland ointment is recommended after the patient has been removed from the scene of exposure at least 24 hours.

Local Anesthetics. Because of the marked edema of the lids, intense blepharospasm and photophobia which follows moderately severe exposure to mustard, the patient cannot open his eyes voluntarily and so may fear that he has been permanently blinded. The lids should be opened up to demonstrate to the patient that his sight has not been lost. To facilitate the examination or treatment of such a patient, it is often necessary to instil a local anesthetic. All local anesthetics inhibit the respiration of the cornea and reduce the regenerative power of the epithelium. After several instillations of any local anesthetic into a normal eye, the cornea will show some punctate staining when tested with fluorescein. Such damage to the corneal epithelium will accelerate the penetration of any toxic agent. Cocaine 2% is universally stated to be the worst offender, and other local anesthetics have been recommended in its place: e.g., holocaine 1%, butyn 2%, or pontocaine $\frac{1}{2}$ %. Local hypersensitivity to butyn develops not infrequently, and therefore pontocaine is becoming more widely favored in ophthalmologic circles as a local anesthetic agent.

The question arises whether the moderate use of local anesthetics should be absolutely contraindicated in the treatment of ocular burns by vesicant war gases. Animal experiments indicate that a few drops of pontocaine $\frac{1}{2}$ % has no significant detrimental effect on the course of mustard or Lewisite lesions. However, several instillations over the course of an hour apparently lowers the resistance of the eye to Lewisite burns.

I think we can conclude that the use of a local anesthetic is not detrimental if necessary for examination or treatment of the patient, but should not be used repeatedly as a mode of treatment.

Secondary Iritis. Iritis is found in all severely burned eyes. To dilate the pupil and prevent the formation of adhesions between the iris and lens, atropine sulfate 1% should be instilled at the time of the first examination and continued three times a day until the iritis subsides. Homatropine 2% may be used in less severe cases in which there is photophobia and reflex miosis resulting from severe irritation of the conjunctiva and cornea. The fear of glaucoma resulting from the use of atropine in older individuals is less important than the serious complications ensuing from a poorly dilated pupil.

Secondary Infection. Streptococci have been found to grow better in eyes which have previously been burned with mustard. Also, in mustard casualties of the last war, late corneal infiltration and ulceration was commonly attributed to the development of secondary in-

Gas poisoning damages the bone marrow, with resulting leucopenia and a reduced titer of circulating antibodies in the blood stream. However, Leber showed in 1891 that a purulent reaction can be elicited by mustard gas alone, without the presence of any secondary infection.

The instillation of argyrol 10% followed by irrigation with a 2% solution of boric acid to remove discharge reduces the likelihood of secondary infection. Sulfonamide drops and ointments have been widely used in the treatment of conjunctivitis and corneal ulcers. The English recommend the instillation of "Albucid" (sulfacetamide) 2.5% solution in the treatment of mustard burns. This sulfanilamide derivative is not considered by many in America to be the most effective. Instead, a finely ground sulfathiazol or sodium sulfadiazine made into a 5% ointment with some bland base such as petrolatum-lanolin (50-50), aquaphor, or K-Y jelly has been advocated for the local treatment of certain ocular infections. The following ointment appears to be satisfactory:

Sulfathiazol or Sodium Sulfadiazine	5%
Absorbent Base (Nimco), Oxycholesterol or Anhydrous Lanolin	12%
Distilled Water	25%
White Vaseline	58%

The ordinary 5% sulfadiazine skin ointment should not be used in the eye because it contains a vanishing cream (soap) base. Recently, the results following the instillation of "microcrystalline" sulfadiazine powder have been encouraging. A new preparation, penicillin, has been found to sterilize "coccus" cultures in the eye effectively. Should the eye burned with mustard develop a severe corneal ulceration or panophthalmitis, sulfadiazine should be given orally, on the average of about 4 grams per day for an adult.

LEWISITE; ClCH=CHAsCl_2 ("M 1").

Lewisite was not used during the first World War, but the Japanese have apparently used it in China on several occasions. In comparison with mustard, it is more sharply irritating and produces more rapid destruction of the eye with lower dosages. In rabbits, application of 0.1 mgm. (0.00005 cc.) of liquid Lewisite results in an instantaneous opacification at the site of contact and the subsequent development of a devastating ocular lesion. This size droplet is what might be expected should Lewisite be disseminated as a fine spray. Equally severe lesions follow exposure of a rabbit's eye to a saturated vapor of Lewisite for 15-30 seconds at room temperature (22-24°C).

Comparison of Severe Mustard and Lewisite Burns of the Eye

<u>Characteristic</u>	<u>Mustard</u>	<u>Lewisite</u>
Latent Period	2-24 hrs. (Vapor) 0 (Liquid)	0-2 min. (Vapor & Liquid)
Conjunctival Reaction	+++	++++
Redness	++	+++
Edema	+++	++++
Necrosis	+++	++++
Corneal Reaction	++	++++
Edema	++	++++
Vascularization	++	+++
Ulceration	++	+++
Residual Opacity	++	+++
Purulent Discharge	++	++++
Iritis	++	++ (exudative)
Relapses	++	0 (?)

Clinical Course. (Slides #32-41). This series of eyes was exposed for 30 seconds to a saturated vapor of Lewisite at 23°C, about one-half the time required to produce a sizable mustard lesion of the eye. Within 30 minutes, edema of the conjunctiva appears and, within an hour or two, becomes so marked that the eyelids cannot be opened easily. At 6 hours, many petechial hemorrhages appear in the conjunctiva; the cornea appears mildly hazy and edematous; and a fibrinous iritis has developed. By 24 hours, much of the corneal epithelium has been desquamated, and the edematous thickening of the stroma may become so extreme that the anterior chamber is abolished. The conjunctival reaction largely subsides by the 4th or 5th day, at which time blood vessels enter the cornea from the limbus. Deep corneal ulceration may develop during the second week, often leading to perforation and phthisis bulbi. Healing of the cornea takes place by a proliferation of fibrous tissue and blood vessels, giving rise to a permanently opaque scar. This progressively downhill course of severe Lewisite burns is usually attended by a profuse mucopurulent discharge. Relapses and recurrent lesions in old Lewisite scars have not been described.

Pathology of Lewisite Burns of the Rabbit's Eye. Ten minutes after a small droplet (0.1 mgm.) of Lewisite has been applied to the limbal region of a rabbit's eye, histological examination reveals a slight edema of the corneal epithelium, swelling of the stromal cells, and some serum in the anterior chamber. At one hour, the conjunctiva shows marked edema with congestion of the vessels and the migration of a few polymorphonuclear cells outside the walls of the blood vessels. Occasionally serous fluid may separate the corneal epithelium from

the stroma (a type of vesicle). The nuclei of the involved stromal cells are pyknotic. Serum is present in the anterior chamber and the vessels in the iris are congested. At 4 hours, the conjunctiva has become heavily infiltrated with polys, and red blood cells have extravasated into the edematous tissue. The cornea shows some infiltration by polys near the limbus, and the edema of the stroma has increased. Hemorrhages appear in the iris and many of the vessels are thrombosed. At 10 hours, the surface of the cornea is partially devoid of epithelium. A few polys can be seen in the anterior chamber. At 24 hours, most of the conjunctival epithelium has sloughed off. The entire cornea is edematous and few if any stromal cells can be found remaining in the most severely burned portion. The anterior chamber is filled with fibrin and purulent exudate. At 4 days, most of the corneal epithelium has regenerated as a single layer of cells, unless secondary infection or marked sloughing has occurred. Polys have by this time migrated extensively into the corneal stroma. The iris pigment is disorganized. At 7 days, small capillaries are present within the cornea, near the corneo-scleral junction. At 10 days, a heavy pannus formation of vessels extends deeply into the cornea. Most of the polymorphonuclear reaction is replaced by mononuclear cells and a few fibroblasts. The anterior chamber exudate and most of the iritis have subsided. After 12 days, unless the eye perforates and becomes phthisical, the cornea is repaired by an exuberant growth of blood vessels and fibrous tissue. This often blocks the drainage angle of the anterior chamber, predisposing to the development of secondary glaucoma.

In summary, we find an extremely rapid penetration of Lewisite with necrosis of all the cells in the conjunctiva, cornea, iris and blood vessels. This is associated with the development of a marked edema of conjunctiva and cornea. After a few hours, a purulent reaction appears with the formation of an exudative iritis. This is largely replaced by a mononuclear reaction and fibrous tissue formation, associated with vascularization of the cornea after one week. Some of the eyes heal with this opaque scar tissue formation, although perforation is very common.

Treatment of Lewisite Burns of the Eye. Toxic arsenical material can be demonstrated to have disappeared from the surface of the eye and to have penetrated through the cornea and into the anterior chamber within 2 minutes after exposure to M 1 vapor or liquid. In accordance with these facts, experiments have shown that efforts to decontaminate the eye by irrigations or by solutions of hydrogen peroxide and potassium permanganate (which do not penetrate well and are themselves toxic to the cornea) come to naught. Fortunately, contact with either Lewisite vapor or liquid affords immediate warning to the victim that he has been burned.

An antidote of secret formula has recently been discovered to be effective in the early treatment of Lewisite burns of the eye.

This is called either "M 1 Eye Solution", or it may later be put out as "BAL Ointment". There are two important directives to be considered: (1) M 1 Eye Solution is toxic in itself, and if used excessively in the eye, can produce marked damage. One drop of the antidote affords maximum protection, although two or three drops will not injure the eye. The instillation should not be repeated. About 0.1 to 0.2 cc. of the ointment is adequate.

(2) M 1 Eye Solution becomes progressively less effective as time elapses after exposure. It is impossible to revive a dead cell. Treatment within two minutes of exposure gives complete protection, treatment after 5 minutes affords somewhat diminished protection, after 10 minutes greatly diminished effect, after 30 minutes very little benefit, and after 45 minutes is contraindicated. The solution or ointment will probably be issued in small packages so that it will be immediately available for instillation into the eye before adjusting the gas mask. Because the material is somewhat irritating to the normal eye, it is not recommended for prophylaxis.

If treatment has not been instituted within the first hour after exposure, subsequent measures should follow those outlined for mustard.

"N-Mustard". This new vesicant war gas attacks the eyes, respiratory tract, and has general systemic toxicity. Devastating lesions of the eye are produced by a 15 to 30 second exposure to a concentrated vapor at 23°C. They are characterized by a relatively slow onset and few conjunctival signs, but most of the cells in the blood vessels, cornea and iris are killed within half an hour after such an exposure. The cornea develops an increasingly dense opacification for the first week, after which a relentless ulceration and vascularization ensues. The onset of symptoms resembles that of mustard-burned eyes, but the ultimate damage to the eye is more characteristic of Lewisite.

No specific treatment has been discovered. In order to prevent secondary complications, the outline for the treatment of mustard burns should be followed.

TEAR GAS OR CHLORACETOPHENONE. $\text{C}_6\text{H}_5\text{C}(=\text{O})\text{ClCH}_2$

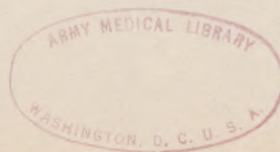
Tear gas produces a self-limited irritation of the conjunctiva and cornea with reflex lacrimation and photophobia. Vapor produces no permanent ocular lesion. Treatment consists in: (1) Gas mask, or evacuation from the contaminated area. (2) Irrigations of the eye with a bland solution. (3) Instillations of 0.4% sodium sulfite in 75% glycerin (McNally).

SUMMARY. With the exception of specific treatment of early Lewisite burns of the eye with "M 1 Eye Solution", the following regime may be followed as an effort to ameliorate the symptoms

and prevent secondary complications.

GENERAL TREATMENT OF VESICANT WAR GAS INJURIES TO THE EYES

1. Irrigation within 3 minutes after burns by liquid vesicants with water or any non-irritating solution such as 1.5% sodium bicarbonate, 2% boric acid, or 0.9% saline. Vapor burns should not be irrigated for decontamination purposes.
2. Reassurance of the patient that he is not blind by opening his eyes.
3. Pontocaine $\frac{1}{2}\%$, butyn 1%, or cocaine 2% only if necessary for examination or performing treatments.
4. Evacuation of patients with corneal burns to the ophthalmologic service. These patients (not those with minor conjunctival involvement) should receive the following treatment:
 - 4a. Atropine sulfate 1% solution or ointment three times a day.
 - 4b. Experimental use of a 5% sulfathiazol or sodium sulfadiazine ointment (in a bland base such as petrolatum-lanolin (50-50), aquaphor, or K-Y jelly base) every 4 hours beginning 24 hours after the exposure. Do not use the 5% sulfadiazine skin ointment in the eye. "Microcrystalline" sulfadiazine powder or penicillin may be tried. For corneal ulceration, use sulfadiazine orally (about 4 grams per day for an adult).
5. Dark glasses or eyeshade if necessary for severe photophobia. Pressure bandage may be used during the healing stage of corneal ulceration, but bandaging cases with conjunctival lesions only is definitely disadvantageous.
6. Boric acid or saline irrigations only when needed to remove mucopurulent discharge.
7. Zinc sulfate 1/4% with adrenalin (3 i of 1/1000 to 3 i) three times a day during convalescence.



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